

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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RECEIVED

- 8 OCT 2004

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PCT

WRITTEN OPINION  
(PCT Rule 66)

Date of mailing  
(day/month/year)

08.10.2004

Applicant's or agent's file reference  
CDMP61500/001

**REPLY DUE within 1 month(s) and 15 days**  
from the above date of mailing

International application No.  
PCT/GB 03/03686

International filing date (day/month/year)  
22.08.2003

Priority date (day/month/year)  
23.08.2002

International Patent Classification (IPC) or both national classification and IPC  
C07H21/00

Applicant  
SOLEXA LIMITED

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.
 

**When?** See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also:** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed,** the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 23.12.2004

Name and mailing address of the international preliminary examining authority:



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**I. Basis of the opinion**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

**Description, Pages**

1-116 as originally filed

**Claims, Numbers**

1-50 as originally filed

**Drawings, Sheets**

1-7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-2 (in part), 3-4 (in full), 5-11 (in part), 12-28 (in full), 29-50 (in part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-2 (in part), 3-4 (in full), 5-11 (in part), 12-28 (in full), 29-50 (in part)

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-2, 5-7, 9-10, 29-30, 34-36, 40-50
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Inventive step (IS)	Claims	1-2, 5-7, 9-10, 29-31, 34-37, 40-50
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Industrial applicability (IA)	Claims	
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2. Citations and explanations

**see separate sheet**

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Note that this examination is only for claims 1-2, 5-11, 29-50 (all in part) for which the modified nucleotide or nucleoside is as claimed in claim 1 where Z is  $-C(R')_2-O-R''$  with R' and R'' as in claim 1, and methods and kits pertaining thereto, since no search report was established for the other parts of the claims.

Reference is made to the following documents:

D1: WO0229003

D2: US6255475

D3: J. Brunckova et al. Tetrahedron Letters 35 (1994) 6619-6622

D4: S. Nishino et al. Heteroatom Chemistry 2 (1991) 187-196

D5: M. Krecmerova et al. Collect. Czech. Chem. Commun. 55 (1990) 2521-2536

D6: J.-I. Yamashita et al. Chem. Pharm. Bull. 35 (1987) 2373-2381

D7: DE19611759

The document D7 was not cited in the international search report. A copy of the document is appended hereto.

**Novelty**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-2, 5-7, 9-10, 29-30, 34-36, 40-50 is not new in the sense of Article 33(2) PCT.

The documents D1-D6 disclose compounds (D1: Figures, pertinent to claim 1; D2: Figures 2 and 4, pertinent to claims 1 and 2; D3: compounds 10a-c, pertinent to claims 1 and 2; D4: Scheme 2, pertinent to claims 1 and 2; D5: compounds at pages 2522-2523, pertinent to claims 1 and 5; D6: tables, pertinent to claims 1,2,5) falling within the scope of claims 1,2 and 5. These claims are therefore lacking novelty.

The compounds of D1 are linked via its base through cleavable and non-cleavable linkers to detectable labels. Thus, claims 6, 7, 9 and 10 are also lacking novelty.

The compounds of D1 are used in sequencing using polymerases, thus claims 29, 30, 34-36, 40-50 also lack novelty.

**Inventive step**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 6-7, 9-10, 29-30, 34-36, 40-50 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 1, 6-7, 9-10, 29-30, 34-36, 40-50 and discloses the same solution to the same problem as in the present application. Thus, no inventive step is present in those claims.

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 31 and 37 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 31 and 37, and discloses modified nucleosides for use in sequencing reactions using polymerases.

The subject-matter of claims 31 and 37 therefore differs from this known subject matter in that the polymerase is a *Thermococcus* sp.

The problem to be solved by the present invention may therefore be regarded as provision of a further polymerase for a sequencing reaction.

The solution proposed in claims 31 and 37 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons. From D7 it is known that enzymes from *Thermococcus* sp. can be used as polymerases. Combination of D1 and D7 would thus give the same solution to the above problem as in the present application.